## REMARKS

Claims 34-39, 41 and 42 will be pending upon entry of the presently made amendments.

New claims 41 and 42 have been added. Support for new claims 41 and 42 is found in the specification as filed at least at page 6, line 12 to page 7, line 15. No new matter has been added.

Applicants reserve the right to prosecute the subject matter of any previously canceled, withdrawn or amended claim or any other unclaimed subject matter in one or more continuation, divisional or continuation-in-part applications.

### I. Abstract

It appears that the Examiner did not actually object to the format of the Abstract. Accordingly, Applicants have not addressed this section of the Office Action. Applicants respectfully seek confirmation that their understanding is correct.

### II. Rejection of Claims 34-39 Under the Judicially Created Doctrine of Obviousness-Type Double Patenting over U.S. Patent No. 6,436,923 B1

Claims 34-39 have been rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-49 of U.S. Patent No. 6,436,923 B1 ("the '923 patent"). Applicants respectfully traverse this rejection and submit that this rejection is improper for the reasons set forth below.

A patent issuing on an application with respect to which a requirement for restriction under 35 U.S.C. § 121 was made, or on an application filed as a result of such a requirement, shall not be used as a reference in the Patent and Trademark Office against a divisional application, if the divisional application is filed before the issuance of the patent on the other application. 35 U.S.C. § 121, third sentence. Note M.P.E.P. § 804.01. In other words, 35 U.S.C. § 121 prohibits the use of a patent issuing on an application with respect to which a requirement for restriction was made as a reference against a subsequent divisional application.

The present application is a division of U.S. App. No. 10/085,999, now U.S. Patent No. 6,686,351 B2 ("the '351 patent"), which is a division of U.S. App. No. 09/527,750, now the '923 patent. During prosecution of the '923 patent, a restriction requirement under 35 U.S.C. § 121 was issued wherein election from one of the following seven groups was required:

| | |
|---|---|
| Group I. | Claims 1-33, directed to the compounds of formula in claim 1 wherein A and B are carbon atoms and C is nitrogen; |
| Group II. | Claims 1-33, directed to the compounds of formula in claim 1 wherein A, B, and C are all nitrogens; |
| Group III. | Claims 1-33, directed to the compounds of formula in claim 1 wherein one of A and B is nitrogen and C is nitrogen; |
| Group IV. | Claims 1-33, directed to the compounds not included in Groups I-III; |
| Group V. | Claims 34-39, directed to a method of modulating ER-β; |
| Group VI. | Claims 40 and 41, directed to a method for treating an estrogen-related condition; and |
| Group VII. | Claims 42-44, directed to a method for inhibiting cytokine. |

In response, Applicants elected to prosecute the subject matter of Group I, Claims 1-33, directed to the compounds of formula in claim 1 wherein A and B are carbon atoms and C is nitrogen. This subject matter is now in the '923 patent.

Applicants subsequently filed U.S. App. No. 10/085,999, now the '351 patent, prior to the issuance of the '923 patent, wherein the subject matter of Group III, Claims 1-33, directed to the compounds of formula in claim 1 wherein one of A and B is nitrogen and C is nitrogen was prosecuted. This subject matter is now in the '351 patent.

In the present application, which was filed prior to the issuance of the '351 patent, Applicants are pursuing the subject matter of Group V, Claims 34-39, directed to a method of modulating ER-β.

Accordingly, Applicants submit that it is improper to reject claims 34-39 of the present application under the judicially created doctrine of obviousness-type double patenting over the '923 patent and respectfully request that the rejection be withdrawn.

## III. Rejection of Claims 34-39 Under the Judicially Created Doctrine of Obviousness-Type Double Patenting over U.S. Patent No. 6,686,351 B2

Claims 34-39 have been rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-17 of U.S. Patent No. 6,686,351 B2 ("the '351 patent"). Applicants respectfully traverse this rejection and submit that this rejection is improper for the reasons set forth below.

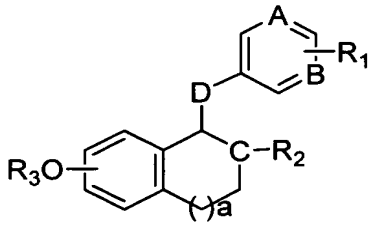
As discussed above, the present application is a division of the '351 patent, which is a division of the '923 patent, wherein a restriction requirement under 35 U.S.C. § 121 was issued in connection with the application which issued as the '923 patent, with one group being prosecuted in the application which issued as the '351 patent and one group being prosecuted in the present application.

Accordingly, for the same reasons set forth above, pursuant to 35 U.S.C. § 121, Applicants submit that it is improper to reject claims 34-39 of the present application under the judicially created doctrine of obviousness-type double patenting over the '351 patent and respectfully request that the rejection be withdrawn.

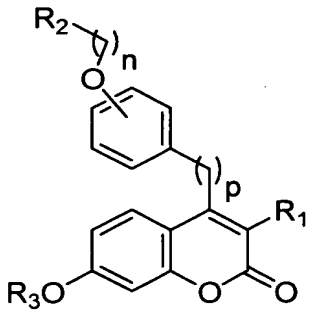
## IV. Rejection of Claims 34-39 Under the Judicially Created Doctrine of Obviousness-Type Double Patenting over U.S. Patent No. 6,372,739 B1

Claims 34-39 have been rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-20 of U.S. Patent No. 6,372,739 B1 ("the '739 patent"). Applicants respectfully traverse this rejection for the reasons set forth below.

The Examiner has stated that claims 34-39 of the present application refer to the same compounds as the '739 patent. Applicants respectfully disagree. Claims 34-39 of the present application are directed to uses of compounds of the following structure:




In contrast, the claims of the '739 patent are directed to compounds of the following structure:




The structures of these compounds differ at least in that the core scaffold of compounds of the '739 patent contain an oxygen, a carbonyl and a double bond in the ring fused to phenyl, whereas the presently claimed compounds do not. Applicants respectfully submit that the compounds of pending claims 34-39 are neither structurally related to nor the same as the compounds claimed in the '739 patent.

Accordingly, Applicants respectfully request that the rejection of claims 34-39 of the present application under the judicially created doctrine of obviousness-type double patenting over the '739 patent be withdrawn.

## V. Rejection of Claims 34-39 Under the Judicially Created Doctrine of Obviousness-Type Double Patenting over U.S. Patent App. No. 10/085,995

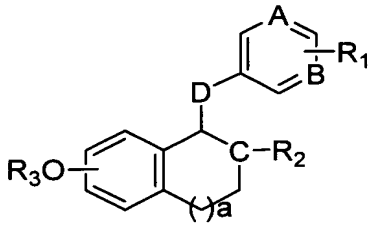
Claims 34-39 have been rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-40 of U.S. Patent App. No. 10/085,995.

In an April 13, 2006 teleconference between Attorney for Applicants Michael J. Bruner and Examiner Shirley Gembeh, Examiner Gambeh confirmed that this was a typographical error and that U.S. Patent App. No. 10/085,999 ("the '999 application") was intended to be cited in this section of the office action. Examiner Gambeh also acknowledged that the '999 application is that which issued as the '351 patent (addressed above in Section III) and, accordingly, indicated that this rejection was duplicative and would be withdrawn.

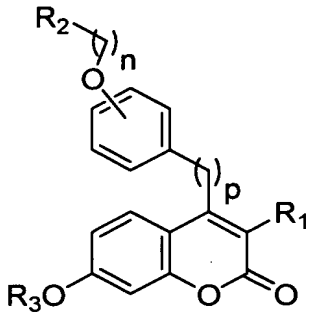
## VI. Rejection of Claims 34-39 Under the Judicially Created Doctrine of Obviousness-Type Double Patenting over U.S. Patent No. 6,291,456 B1

Claims 34-39 have been rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 36-78 of U.S. Patent No. 6,291,456 B1 ("the '456 patent"). Applicants respectfully traverse this rejection for the reasons set forth below.

The Examiner has stated that the present application and the '456 patent recite using the same compositions and/or derivatives thereof. Applicants respectfully disagree. Claims 34-39 of the present application are directed to uses of compounds of the following structure:




In contrast, claims 36-78 of the '456 patent are directed to the use compounds which are encompassed by the following structure:



As discussed above in connection with the '739 patent, the structures of these compounds differ at least in that the core scaffold of the compounds of the '456 patent contain an oxygen, a carbonyl and a double bond in the ring fused to phenyl, whereas the presently claimed compounds do not. Applicants respectfully submit that the compounds of pending claims 34-39 are neither structurally related to nor the same as the compounds set forth in claims 36-78 in the '456 patent.

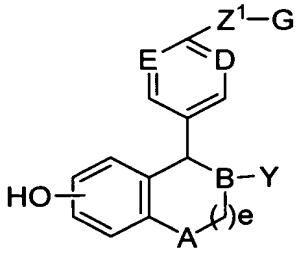
Accordingly, Applicants respectfully request that the rejection of claims 34-39 of the present application under the judicially created doctrine of obviousness-type double patenting over the '456 patent be withdrawn.

## VII. Rejection of Claims 34-39 Under 35 U.S.C. § 102 over U.S. Patent No. 5,552,412 to Cameron

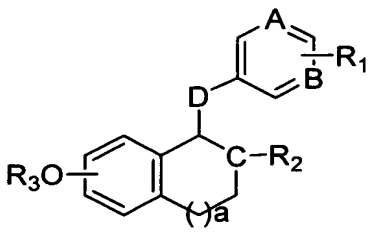
Claims 34-39 have been rejected under 35 U.S.C. § 102(b) as being allegedly unpatentable over U.S. Patent No. 5,552,412 to Cameron ("Cameron"). Applicants respectfully traverse this rejection for the reasons set forth below.

A claim is anticipated only if each and every element as set forth in the claim is found in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987).

Cameron is directed to compounds having the following structure:



These are compounds wherein the bicyclic moiety is directly bonded to the aryl ring. In contrast, the claims of the present application are directed to uses of compounds of the following structure:




wherein the variable D is defined as $-(CH_2)_r-$ or $-(CH_2)_nC(=O)(CH_2)_m-$, wherein *r* is 1, 2, 3, 4 or 5. The bicyclic moiety of the compounds of the presently claimed methods of use cannot being directly bonded to the aryl group (*i.e.*, there must be at least a $-CH_2-$ linker present). Thus, there is no overlap between the compounds of Cameron and the compounds of the presently claimed methods of use and, accordingly, no compound of Cameron anticipates the present method of use claims. *Id.* Accordingly, Applicants respectfully submit that the rejection of claims 34-39 under 35 U.S.C. § 102(b) over Cameron cannot stand and should be withdrawn.

## VIII. Rejection of Claims 34--39 Under 35 U.S.C. § 103 over U.S. Patent No. 5,552,412 to Cameron in view of U.S. Patent No. 6,291,456 B1

Claims 34-39 have been rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Cameron in view of the '456 patent. Applicants respectfully traverse this rejection for the reasons set forth below.

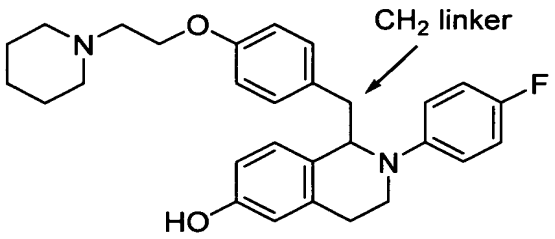
In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the cited reference or generally known to one of ordinary skill in the art, to modify the reference to arrive at the claimed compounds. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). As discussed above in Section VII, the compounds of Cameron differ from the compounds of the present method of use claims at least because the bicyclic moiety of the core structure is directly bonded to the aryl group, wherein the compounds of the present method of use claims require at least a $-CH_2-$ linker between these groups. Applicants respectfully submit that there is no suggestion or motivation to modify the compounds of Cameron, either alone or in view of the '456 patent[1], to arrive at the

[1] As discussed above in Section VI, Applicants respectfully submit that the '456 patent does not disclose compounds which are structurally related to the compounds of the presently claimed methods of use.

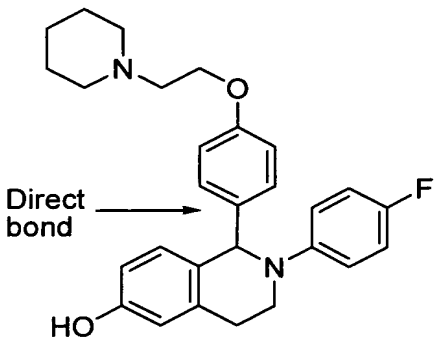
compounds of the present method of use claims. Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

Nevertheless, Applicants respectfully submit that the data set forth in Example 140 at pages 141-143 of the present application overcomes even a *prima facie* case of obviousness over Cameron, either alone or in view of the '456 patent.

In particular, Example 140 sets forth biological data comparing the selectivity for ER-β over ER-α of the compound of Example 5 of the present application to Compound A of PCT International Patent Publication No. WO 96/21656 to Cameron *et al.* (*i.e.*, the international counterpart of Cameron). The compound of Example 5 of the present application has the following structure:




Compound A of PCT International Patent Publication No. WO 96/21656 to Cameron *et al.* has the following structure:




As indicated by the structures set forth directly above, the sole structural difference between these compounds is that Compound A of PCT International Patent Publication No. WO 96/21656 to Cameron *et al.* is that wherein there is a direct bond between the bicyclic moiety and the phenoxy group, whereas the compound of Example 5 of the present application possesses a -$CH_2$- linker at that position. The data set forth in Table 4 of Example 140 demonstrates that Compound A of Cameron is selective for ER-α, whereas the compound of Example 5 of the present invention is selective for ER-β. Applicants note that

claims 34-39 of the present application are directed to methods of use associated with ER-β. In addition, the compounds of Examples 2 and 8 of the present application, which also possess a $-CH_2-$ linker at that position, show selectivity for ER-β over ER-α. Accordingly, this data demonstrates that the structural differences between the compounds of method of use claims 34-39 and the compounds of Cameron are responsible for unexpected changes in biological activity. Applicants respectfully submit that this surprising and unexpected result overcomes even a *prima facie* case of obviousness of claims 34-39 over Cameron in view of the'456 patent. *In re Chupp*, 816 F.2d 643, 646 (Fed. Cir. 1987); *In re May*, 574 F.2d 1082, 1093 (C.C.P.A. 1978).

Accordingly, in view of the above remarks, Applicants respectfully submit that the rejection of claims 34-39 under 35 U.S.C. § 103 over Cameron in view of the'456 patent has been overcome and should be withdrawn.

**Conclusion**

No fee is believed to be due in connection with this response other than that due in connection with the Petition for Extension of Time; however, should the USPTO determine that any additional fee is required, Applicants hereby authorize that the required fee be charged to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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By: Michael J. Bruner, Reg. No. 47,458

Date: July 7, 2006

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